

REMARKS

Applicants have amended claims 1, 2, 4, 8, 11, 15, 23, 25, 27, 29, 39, 59, 60, 63 and 68 to correct typographical errors. Attached hereto is Appendix A, which contains a marked-up version of the changes made to the claims. No new matter has been added. It is respectfully requested that these amendments be considered and entered prior to issuance of a patent corresponding to the present application.

If any fee due is not accounted for herein, please charge such fee to Deposit Account No. 19-3880. If any extension of time is required and not petitioned for, such extension is hereby petitioned for, and it is requested that any fee due in connection therewith be charged to the aforementioned Deposit Account.

Respectfully submitted,



Rena Patel, Ph.D.
Attorney for Applicants
Reg. No. 41,412

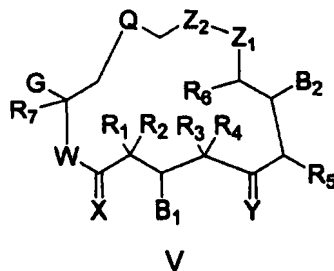
Date: April 1, 2003

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-5398

Appendix A

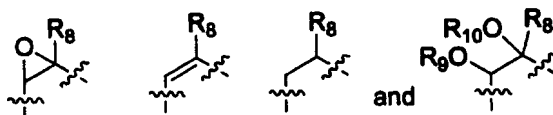
Version With Markings To Show Changes Made

1. (amended) A compound of the formula

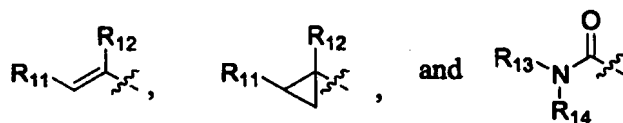


wherein:

Q is selected from the group consisting of



G is selected from the group consisting of alkyl; substituted alkyl; substituted aryl; a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;



W is O or NR₁₅;

X is O or H, H;

Y is selected from the group consisting of O; H, OR₁₆; OR₁₇, OR₁₇; NOR₁₈; [H, NOR₁₉] H, NHOR₁₉; H, NR₂₀R₂₁; H, H; and CHR₂₂; wherein OR₁₇, OR₁₇ can be a cyclic ketal;

Z₁ and Z₂ are independently CH₂;

B₁ and B₂ are independently selected from the group consisting of OR₂₄, OCOR₂₅, and O-C(=O)-NR₂₆R₂₇, and when B₁ is OH and Y is OH, H, they can form a six-membered ring ketal or acetal;

R₁, R₂, R₃, R₄, R₅, R₇, R₁₃, R₁₄, R₁₈, R₁₉, R₂₀, R₂₁, R₂₂, R₂₆, and R₂₇ are selected from the group consisting of H, alkyl, substituted alkyl, and aryl, and when R₁ and R₂ are alkyl can be joined to form a cycloalkyl; and when R₃ and R₄ are alkyl can be joined to form a cycloalkyl;

R₆ is methyl;

R₉, R₁₀, R₁₆, R₁₇, R₂₄, R₂₅ and R₃₁ are selected from the group consisting of H, alkyl, and substituted alkyl;

R₁₁, R₁₂, R₂₈, R₃₀, R₃₂, and R₃₃ are selected from the group consisting of H; alkyl; substituted alkyl; aryl; substituted aryl; cycloalkyl containing 1 to 3 rings and 3 to 7 carbons per ring which may be further fused with an unsaturated C₃-C₇ carbocyclic ring; and [heterocycle] a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;

R₈ is hydrogen or methyl;

R₁₅, R₂₃ and R₂₉ are selected from the group consisting of H; alkyl; substituted alkyl; aryl; substituted aryl; cycloalkyl containing 1 to 3 rings and 3 to 7 carbons per ring which may be further fused with an unsaturated C₃-C₇ carbocyclic ring; a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur; R₃₂C=O, R₃₃SO₂, hydroxy, O-alkyl or O-substituted alkyl;

or pharmaceutically acceptable salts, hydrates, solvates or geometric, optical or stereoisomers thereof;

with the proviso that compounds wherein

W and X are both O; and

R₁, R₂ and R₇ are H; and

R₃, R₄ and R₆ are methyl; and

R₈ is H or methyl; and

[Z₁, and Z₂, are CH₂; and]

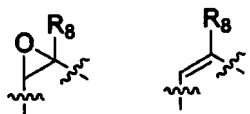
G is 1-methyl-2-(substituted-4-thiazolyl-ethenyl; and

Q is as defined above

are excluded.

2. (amended) The compound of claim 1, wherein

Q is



X is [0] Q;

Y is [0] Q;

Z₁, and Z₂, are CH₂; and

W is NR₁₅.

4. (amended) A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, [prostrate] prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 1.

8. (amended) A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, [prostrate] prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 2.

11. (amended) A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, [prostrate] prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 3.

15. (amended) A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, [prostrate] prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 14.

23. (amended) A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, [prostrate] prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 19.

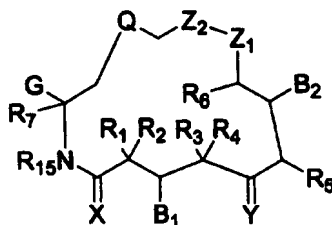
25. (amended) A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, [prostrate] prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 20.

27. (amended) A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, [prostrate] prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 21.

29. (amended) A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, [prostrate] prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 22.

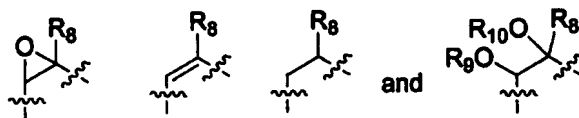
39. (amended) The method of claim 4, further comprising administering one or more of [a] an additional anti-cancer agent.

59. (amended) A compound of the formula:

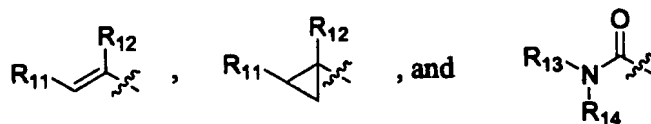


wherein:

Q is selected from the group consisting of



G is selected from the group consisting of alkyl; substituted alkyl; substituted aryl; a 4 to 7 membered monocycle, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;



X is O or H, H;

Y is selected from the group consisting of O; H, OR₁₆; OR₁₇, OR₁₇; NOR₁₈; [H, NOR₁₈] H, NHOR₁₉; H, NR₂₀R₂₁; H, H; and CHR₂₂; wherein OR₁₇, OR₁₇ can be a cyclic ketal;

Z₁ and Z₂ are independently CH₂;

B₁ and B₂ are independently selected from the group consisting of OR₂₄, OCOR₂₅, and O-C(=O)-NR₂₆R₂₇, and when B₁ is OH and Y is OH, H they can form a six-membered ring ketal or acetal;

R₁, R₂, R₃, R₄, R₅, R₇, R₁₃, R₁₄, R₁₈, R₁₉, R₂₀, R₂₁, R₂₂, R₂₆, and R₂₇ are selected from the group consisting of H, alkyl, substituted alkyl, and aryl, and when R₁ and R₂ are alkyl can be joined to form a cycloalkyl; and when R₃ and R₄ are alkyl can be joined to form a cycloalkyl;

R₆ is methyl;

R₉, R₁₀, R₁₆, R₁₇, R₂₄, R₂₅ and R₃₁ are selected from the group H, alkyl, and substituted alkyl;

R₁₁, R₁₂, R₂₈, R₃₀, R₃₂, and R₃₃ are selected from the group consisting of H; alkyl; substituted alkyl; aryl; substituted aryl; cycloalkyl containing 1 to 3 rings and 3 to 7 carbons per ring which may be further fused with an unsaturated C₃-C₇ carbocyclic ring; and a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;

R₈ is hydrogen or methyl;

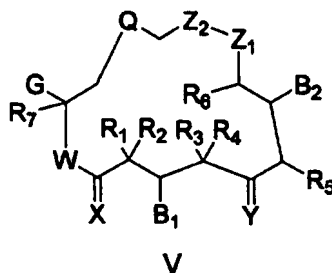
R₁₅, R₂₃ and R₂₉ are selected from the group consisting of H; alkyl; substituted alkyl; aryl; substituted aryl; cycloalkyl containing 1 to 3 rings and 3 to 7 carbons per ring which may be further fused with an unsaturated C₃-C₇ carbocyclic ring; a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur; R₃₂C=O, R₃₃SO₂, hydroxy, O-alkyl or O-substituted alkyl;

or pharmaceutically acceptable salts, hydrates, solvates or geometric, optical or stereoisomers thereof.

60. (amended) A method of treating breast cancer, ovarian cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, [prostrate] prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 59.

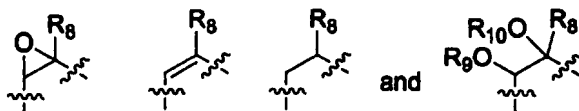
63. (amended) The method of claim 60, further comprising administering one or more of [a] an additional anti-cancer agent.

68. (amended) A compound of the formula:

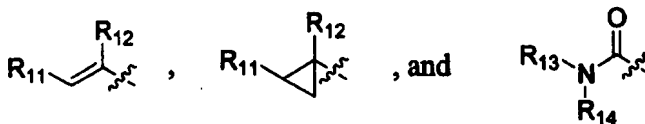


wherein:

Q is selected from the group consisting of



G is selected from the group consisting of alkyl; substituted alkyl; substituted aryl; a 4 to 7 membered monocycle, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;



W is O or NR₁₅;

X is O or H, H;

Y is selected from the group consisting of O; H, OR₁₆; OR₁₇, OR₁₇; NOR₁₈; [H, NOR₁₉] H, NHOR₁₉; H, NR₂₀R₂₁; H, H; and CHR₂₂; wherein OR₁₇, OR₁₇ can be a cyclic ketal;

Z₁ and Z₂ are independently CH₂;

B₁ and B₂ are independently selected from the group consisting of OR₂₄, OCOR₂₅, and O-C(=O)-NR₂₈R₂₇, and when B₁ is OH and Y is OH, H they can form a six-membered ring ketal or acetal;

R₁, R₂, R₃, R₄, R₅, R₇, R₁₃, R₁₄, R₁₈, R₁₉, R₂₀, R₂₁, R₂₂, R₂₆, and R₂₇ are selected from the group consisting of H, alkyl, substituted alkyl, and aryl, and when R₁ and R₂ are alkyl can be joined to form a cycloalkyl; and when R₃ and R₄ are alkyl can be joined to form a cycloalkyl;

R₆ is methyl;

R₉, R₁₀, R₁₆, R₁₇, R₂₄, R₂₅ and R₃₁ are selected from the group H, alkyl, and substituted alkyl;

R₁₁, R₁₂, R₂₈, R₃₀, R₃₂, and R₃₃ are selected from the group consisting of H; alkyl; substituted alkyl; aryl; substituted aryl; cycloalkyl containing 1 to 3 rings and 3 to 7 carbons per ring which may be further fused with an unsaturated C₃-C₇ carbocyclic ring; and a 4 to 7 membered monocyclic, 7

to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur;

R₈ is hydrogen or methyl;

R₁₅, R₂₃ and R₂₉ are selected from the group consisting of H; alkyl; substituted alkyl; aryl; substituted aryl; cycloalkyl containing 1 to 3 rings and 3 to 7 carbons per ring which may be further fused with an unsaturated C₃-C₇ carbocyclic ring; a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic saturated or unsaturated ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur; R₃₂C=O, R₃₃SO₂, hydroxy, O-alkyl or O-substituted alkyl;

or pharmaceutically acceptable salts, hydrates, solvates or geometric, optical or stereoisomers thereof;

wherein substituted alkyl is an alkyl group substituted with from one to four substituents selected from the group consisting of halo; trifluoromethyl; trifluoromethoxy; hydroxy; alkoxy; cycloalkoxy; heterocyclooxy; oxo; alkanoyl; aryloxy; alkanoyloxy; amino; alkylamino; arylamine; aralkylamino; cycloalkylamino; heterocycloamino; disubstituted amines wherein the substituents are selected from alkyl, aryl, and aralkyl; alkanoylamino optionally substituted with halogen, alkyl, alkoxy, aryl, or aralkyl; arylamino optionally substituted with halogen, alkyl, alkoxy, aryl, or aralkyl; aralkanoylamino optionally substituted with halogen, alkyl, alkoxy, aryl, or aralkyl; thio; alkylthio; aralkylthio; cycloalkylthio; heterocyclothio; alkylthiono; arylthiono; aralkylthiono; alkylsulfonyl; arylsulfonyl; aralkylsulfonyl; sulfonamido optionally substituted with halogen, alkyl, alkoxy, aryl, or aralkyl; nitro; cyano; carboxy; carbamyl optionally substituted with halogen, alkyl, alkoxy, aryl, or aralkyl; alkoxycarbonyl; aryl; substituted aryl; granidino; and heterocyclo; and

substituted aryl is an aryl group substituted with from one to four substituents selected from the group consisting of alkyl; substituted alkyl; halo; trifluoromethyl; trifluoromethoxy; hydroxy; alkoxy; cycloalkoxy; heterocyclooxy; alkanoyl; alkanoyloxy; amino; alkylamino; aralkylamino; cycloalkylamino; heterocycloamino; dialkylamino; alkanoylamino; thio; alkylthio; cycloalkylthio; heterocyclothio; ureido; nitro; cyano; carboxy; carboxyalkyl; carbamyl; alkoxycarbonyl; alkylthiono; arylthiono; alkylsulfonyl; sulfonamido; and aryloxy each of which may be optionally substituted with halo, hydroxy, alkyl, alkoxy, substituted aryl, substituted alkyl, or substituted aralkyl;

with the proviso that compounds wherein

W and X are both O; and

R₁, R₂ and R₇ are H; and

R₃, R₄ and R₆ are methyl; and

R₈ is H or methyl; and

G is 1-methyl-2-(substituted-4-thiazolyl-ethenyl; and

Q is as defined above
are excluded.